see commentary on page 247

Atrial fibrillation in incident dialysis patients

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Despite the importance of cardiovascular disease in dialysis patients, the frequency of atrial fibrillation in incident dialysis patients has not been determined. We analyzed the prevalence of atrial fibrillation in patients starting dialysis over a 4-year period, its occurrence over the course of dialysis, and its influence on ischemic stroke and mortality. Factors predisposing to atrial fibrillation were noted, as was the influence of arrhythmia on mortality and presentation of ischemic stroke. Of the 256 patients studied, 31 had atrial fibrillation at the start of dialysis. Increased age, larger left atrium, and female gender were independently related to the presence of atrial fibrillation at dialysis inception. Of the 225 patients who were in sinus rhythm at the start of dialysis, 28 developed atrial fibrillation during a mean follow-up time of 2 years. The presence of valvular calcifications, bundle branch block, previous ischemic stroke, lower ejection fraction, higher pulse pressure, and lower hemoglobin concentration were predictors of the clinical evolution of atrial fibrillation. Overall, atrial fibrillation increased mortality risk 1.72-fold and ischemic stroke risk 9.8-fold. Therefore, it appears that atrial fibrillation is quite prevalent and its presence is associated with significant risk.

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The importance of cardiovascular disease in dialysis patients with chronic renal insufficiency is currently well established. Cardiovascular disease constitutes the principal cause of death in this population group.[1,2] Atrial fibrillation (AF) is the sustained arrhythmia most frequently encountered in routine clinical practice in the general population, but it also represents an important social and health-care problem.[3,4]

Despite this, AF in dialysis patients has only recently merited some attention in the medical literature.[5,6] Over the past few years, there have been studies that have evaluated this arrhythmia in this patient population, and the findings indicate that it is a very frequent disease with a prevalence that varies between 11 and 27%,[7–9] and with an annual incidence of between 3.1 and 4.1 in patients on dialysis treatment.[10,11] However, there is not a single study that has evaluated the prevalence of AF in patients commencing dialysis, or of its incidence in the course of the clinical evolution of dialysis treatment.

The objective of this study was to analyze the prevalence of AF in patients starting dialysis, to determine its incidence in the course of dialysis in those not identified as having AF at the start of dialysis, and to establish the influence of AF on stroke and mortality.

RESULTS

There were 333 patients who commenced dialysis in our center over the recruitment period. Of these, nine recovered renal function, 14 were referred to us from another center, 25 had received a previous transplant, and 29 died early or had changed their residence outside our catchment area. The remaining 256 patients were included in this study. The clinical characteristics and the echocardiographic data are summarized in Table 1.

Prevalence of AF

Of the 256 patients, 31 (12.1%) were diagnosed as having AF in one or other of its clinical manifestations. Of these, 19 (7.4%) had permanent AF and there had been an earlier episode documented in 12 (4.7%). The patients with AF were predominantly women, older age group, higher body mass index, greater left ventricular hypertrophy, and greater dimensions of the left atrium. The concentrations of creatinine were lower and those of C-reactive protein were higher in the patients with arrhythmia. Of the patients with

Table 1 | Clinical characteristics and hematological, biochemical, and echographic parameters of the overall study group

	All (*n*=256)	SR (*n*=225)	AF (*n*=31)	*P*[a]
Age (years)	65.0 ± 15.9	63.5 ± 16.1	76.7 ± 7.3	0.001
Females (%)	110 (43)	89 (39.5)	21 (67.7)	0.003
Smokers (%)	68 (26.1)	63 (28)	5 (16)	0.161
BMI (kg/m^2)	27.4 ± 5.2	27.1 ± 5.0	29.8 ± 6.0	0.005
Pulse pressure (mm Hg)	55.9 ± 21.3	55.1 ± 21.3	61.9 ± 20.7	0.095
Previous hypertension (%)	214 (83.6)	190 (84.4)	24 (77.4)	0.322
Diabetes on hypoglycemic treatment (%)	73 (28.5)	64 (28.4)	9 (29)	0.946
Hemodialysis treatment (%)	213 (83.2)	186 (82.7)	27 (87)	0.536
Documented previous ischemic stroke or TIA (%)	19 (7.4)	16 (7.1)	3 (9.7)	0.609
Documented previous coronary disease (%)	21 (8.2)	19 (8.4)	2 (6.4)	0.705
Documented previous peripheral embolism (%)	3 (1.2)	1 (0.4)	2 (6.4)	0.004
Bundle branch block (%)	25 (9.8)	21 (9.3)	3 (12.9)	0.530
Hemoglobin (g per 100 ml)	10.6 ± 2.1	10.5 ± 1.5	10.0 ± 1.2	0.068
Platelets ($n \times 10^3/\mu l$)	237 ± 87	241 ± 897	216 ± 678	0.139
Urea (mg per 100 ml)	143.7 ± 51.3	142.8 ± 50	150.8 ± 60	0.416
Creatinine (mg per 100 ml)	6.7 ± 2.3	6.8 ± 2.3	5.6 ± 2.1	0.007
Albumin (g per 100 ml)	3.55 ± 0.54	3.58 ± 0.54	3.38 ± 0.48	0.060
Calcium (albumin corrected) (mg per 100 ml)	9.3 ± 0.9	9.3 ± 0.9	9.4 ± 0.7	0.390
Phosphorus (mg per 100 ml)	5.1 ± 1.7	5.2 ± 1.7	4.6 ± 1.4	0.097
Intact parathormone (pg/ml)	253 ± 247	258 ± 256	209 ± 256	0.304
Ferritin (ng per 100 ml)	315 ± 372	312 ± 360	334 ± 455	0.762
Transferrin (mg per 100 ml)	200 ± 164	200 ± 174	198 ± 47	0.961
Glycosylated hemoglobin (%)	4.63 ± 1.12	4.64 ± 1.14	4.61 ± 0.93	0.878
Homocysteine (μmol/l)	24.4 ± 9.5	24.4 ± 9.3	24.3 ± 11.4	0.958
C-reactive protein (mg per 100 ml)	14.2 ± 24.5	11.9 ± 20.3	30.9 ± 41.2	0.017
Cholesterol (mg per 100 ml)	159 ± 38	160 ± 38	152 ± 35	0.256
Triglycerides (mg per 100 ml)	139 ± 78	140 ± 79	134 ± 73	0.704
Left atrial dimension (mm)	41.3 ± 7.6	40.5 ± 7.3	47.5 ± 6.8	0.000
Ejection fraction (%)	65.0 ± 9.2	65.5 ± 9.1	62.1 ± 9.4	0.060
Ascending aorta dimension (mm)	32.7 ± 3.9	32.8 ± 3.9	32.1 ± 4.2	0.395
LVI mass/body surface (g/m^2)	165.4 ± 52.7	162.0 ± 5.4	191.0 ± 56.1	0.006
E/A ratio mitral filling flow	0.89 ± 0.42	0.89 ± 0.43	0.80 ± 0.33[b]	0.511
Presence of valvular calcifications (%)	128 (50)	103 (45.8)	25 (80.6)	0.000

AF, atrial fibrillation; BMI, body mass index; LVI, left ventricle; SR, sinus rhythm; TIA, transient ischemic attack.
[a]SR vs AF.
[b]Patients with non-permanent AF who were in SR at the time of the evaluation
Analysis of patients with AF vs SR at the start of dialysis. Student's *t*-test or Mann–Whitney test for quantitative variables and Pearson's χ^2-test for qualitative variables.

Table 2 | Factors independently associated with the presence of atrial fibrillation at the start of the dialysis

Variable	Odds ratio	95% CI	*P*
Female gender	2.62	1.03–6.64	0.042
Left atrial dimension	1.13	1.06–1.22	0.001
Age	1.07	1.02–1.13	0.008

CI, confidence interval.
Multivariate logistic regression, including gender, age, body mass index, pulse pressure, left ventricular mass/body surface, left atrial dimension, presence of calcifications, left ventricular ejection fraction, hemoglobin, creatinine, albumin, C-reactive protein, and phosphorus.

arrhythmia, four of every five had annular or valvular calcifications, and two of three embolisms suffered were by patients presenting with AF.

Table 1 summarizes the differences between the patients in whom AF had been identified at the start of the dialysis and those who were in sinus rhythm.

In the multivariate analysis, greater age, greater left atrial dimensions, and female gender were independently associated with the presence of AF at the start of dialysis (Table 2).

Incidence of AF

During follow-up, 86 patients died, five had changed their place of residence out of our clinical catchment area, and 28 received transplants. The mean follow-up in the overall group was 24.22 ± 14.6 months, which represents 516.69 patient-years of follow-up. The mean follow-up of patients in whom AF had not been documented at the start of dialysis ($n = 225$) was 25.08 ± 14.44 months, which represents a follow-up of 470 patient-years. Of these 225 patients, 28 (12.4%) had an episode of AF documented in the follow-up. This represents an incidence of 5.9 per 100 patient-years of follow-up.

The patients who had AF in follow-up (60.7% males) were older, with a higher body mass index, higher pulse pressure, had more ischemic stroke or transient ischemic attack (TIA), and one in every four had presented with bundle branch block. The echocardiographic analysis showed larger dimension of left ventricle, greater hypertrophy of the left ventricle, a lower ejection fraction, and four of every five had valvular calcifications. The hematological and biochemical parameters showed that the patients who developed arrhythmia were more anemic, and had lower concentrations of calcium and

Table 3 | Differences between patients who developed AF over the course of the follow-up and those who maintained sinus rhythm, including statistically significant variables

Variable	SR (*n*=197)	AF (*n*=28)	*P*
Age (year)	61.9 ± 16.4	74.5 ± 8.7	0.001
BMI (kg/m^2)	26.8 ± 4.9	29.1 ± 4.8	0.026
Pulse pressure (mm Hg)	53.3 ± 20.2	67.3 ± 24.6	0.001
LV/BS mass (g/m^2)	158.9 ± 51.1	184.5 ± 48.2	0.017
LVEF (%)	65.9 ± 9.1	62.3 ± 8.9	0.059
LA dimension (mm)	40.1 ± 7.1	43.6 ± 8.4	0.021
Hemoglobin (g per 100 ml)	10.6 ± 1.5	9.9 ± 1.6	0.024
Calcium (albumin corrected) (mg per 100 ml)	9.3 ± 0.9	8.8 ± 0.8	0.009
Albumin (g per 100 ml)	3.6 ± 0.5	3.4 ± 0.5	0.047
Valvular calcifications (%)	80 (40.6)	23 (82.1)	0.001
Bundle branch block (%)	14 (7.1)	7 (25)	0.002
Previous ischemic stroke or transient ischemic attack (%)	11 (5.6)	5 (17.9)	0.018

AF, atrial fibrillation; BS, body surface; BMI, body mass index; LA, left atrium; LV, left ventricle; LVEF, left ventricular ejection fraction; SR, sinus rhythm.
Univariate analysis. Student's *t*-test or Mann–Whitney test for quantitative variables and Pearson's χ^2-test for qualitative variables.

Table 4 | Factors independently associated with the presence of atrial fibrillation over the clinical course of dialysis

Variable	Odds ratio	95% CI	*P*
Valvular calcifications	5.23	1.74–15.67	0.003
Bundle branch block at start of dialysis	5.92	2.22–15.77	0.000
Previous ischemic stroke or transient ischemic attack	3.53	1.12–11.12	0.031
Left ventricle ejection fraction	0.05	0.91–0.99	0.021
Pulse pressure	1.02	1.00–1.03	0.018
Hemoglobin concentration	0.71	0.52–0.97	0.036

CI, confidence interval.
Cox's regression analysis, including age, previous ischemic or transient ischemic attack, calcifications, bundle branch block, body mass index, pulse pressure, left ventricular mass/body surface, left atrial dimension, left ventricular ejection fraction, hemoglobin, albumin-corrected calcium, and albumin.

albumin. Table 3 summarizes the differences between the patients who presented with AF and those who maintained sinus rhythm.

In the multivariate analyses, the variables, such as presence at the start of dialysis of calcifications or bundle branch block, a previous stroke or TIA, lower ejection fraction, a higher pulse pressure, and lower level of hemoglobin, were shown to be independent predictors of AF in the course of the clinical evolution of dialysis (Table 4).

Analysis of mortality

Atrial fibrillation had a significant influence on mortality. A total of 86 patients died during follow-up. Table 5 summarizes the presence of arrhythmia, not only at the start of dialysis but also in the clinical evolution, in patients who died and those who were alive at the end of the study period.

The independent predictors of mortality were the presence of AF irrespective of time of diagnosis, older age, previous stroke or TIA, and a lower concentration of albumin (Table 6).

The survival curves show a clear difference between the patients who presented with AF and those in whom there had not been any episode of arrhythmia detected, either in the overall patient group or when dichotomized with respect to age >65 years (Figure 1).

Table 5 | Differences in the presence of arrhythmia in the patients who died and those who survived over the long term of follow-up

	Dead (*n*=86)	Alive (*n*=170)	*P*
AF at the start of dialysis (*n* (%))	18 (20.9)	13 (7.6)	0.002
AF in the course of dialysis (*n* (%))	18 (20.9)	10 (5.9)	0.001
AF at any period (*n* (%))	36 (41.9)	23 (13.5)	0.001

AF, atrial fibrillation.
Peason's χ^2-test.

Table 6 | Factors independently associated with mortality

Variable	Odds ratio	95% CI	*P*
Previous ischemic stroke or transient ischemic attack	3.31	1.66–6.59	0.001
Age	1.05	1.02–1.07	0.001
Albumin	0.52	0.32–0.84	0.007
AF at any time	1.72	1.06–2.80	0.027

AF, atrial fibrillation; CI, confidence interval.
Cox's regression analysis, including age, hemodialysis vs peritoneal dialysis, previous ischemic stroke or transient ischemic attack, left ventricle ejection fraction, ventricle mass/body surface, left atrial dimensions, calcifications, creatinine, bundle branch block, albumin, AF at any time, and pulse pressure.

Analysis of ischemic stroke

There were seven patients who suffered an ischemic stroke during follow-up. This represents a rate of 1.35 ischemic strokes per 100 patient-years of follow-up. One of these patients had been receiving anticoagulants with an INR (international normalized ratio) within the range programmed (2–3) when the event occurred. Of the 59 patients who had AF at any time during the study, 34 (57.6%) were treated with oral anticoagulants.

Five of the seven patients (71.4%) who suffered an ischemic stroke had been diagnosed as AF at some time in the course of the dialysis. AF irrespective of the time of diagnosis and AF in the course of the dialysis together with previous ischemic stroke, higher number of platelets, and higher hematocrit were related to the presence of ischemic stroke (Table 7).

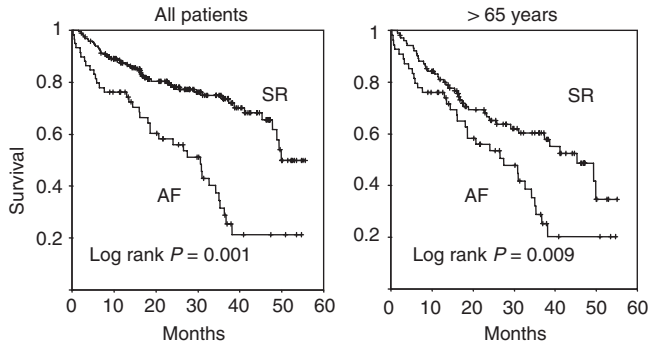

Figure 1 | Survival curves of dialysis patients with AF and those who maintained sinus rhythm (AF, atrial fibrillation; SR, sinus rhythm).

Table 7 | Differences between patients with and without ischemic stroke in the course of the dialysis period

	Ischemic stroke (*n*=7)	No stroke (*n*=249)	*P*
Age (years)	74.7 ± 14.9	64.8 ± 15.9	0.040
Platelets ($n \times 10^3/\mu l$)	309 ± 130	235 ± 85	0.029
Hematocrit (%)	35.1 ± 6.5	31.3 ± 4.6	0.036
Previous ischemic stroke or TIA (*n* (%))	2 (28.6)	17 (6.8)	0.030
AF in the course of dialysis (*n* (%))	3 (42.9)	25 (10)	0.006
AF at any time (*n* (%))	5 (71.4)	54 (21.7)	0.002

AF, atrial fibrillation; TIA, transient ischemic attack.
Univariate analysis. Student's *t*-test or Mann–Whitney test for quantitative variables and Pearson's χ^2-test for qualitative variables.

Table 8 | Factors independently associated with the presence of ischemic stroke in the course of the dialysis period

	Odds ratio	95% CI	*P*
Previous stroke or transient ischemic attack	6.98	1.24–39	0.027
AF at any time	17.3	1.99–150	0.010

AF, atrial fibrillation; CI, confidence interval.
Cox's regression analysis, including age, previous ischemic stroke or transient ischemic attack, AF at any time, hematocrit, platelets, and diabetes.

In the multivariate analyses, AF irrespective of time of diagnosis was the major independent predictor of ischemic stroke presentation, and a higher risk was associated with having had a previous stroke or TIA (Table 8).

The mean follow-up of the patients with AF irrespective of time of diagnosis was 21.39 ± 14.6 months. This represents a follow-up of 105.16 patient-years and a rate of ischemic stroke of 4.75 per 100 patient-years. The mean follow-up of patients who maintained sinus rhythm was 25.06 ± 14.5 months. This represents a follow-up of 411 patient-years and a rate of ischemic stroke of 0.48 per 100 patient-years. As such, the presence of AF implies a 9.8-fold increase in risk of stroke.

DISCUSSION

This study showed a high prevalence and incidence of AF in patients starting dialysis.

The data from this study cannot be compared with other studies as the literature lacks such studies that analyze AF in patients commencing dialysis. When we compare data of prevalence from our population with the general population, we see that AF is present in a higher proportion in the patients who started dialysis.[4,12,13]

In interpreting the high percentage prevalence in our study, we need to take into account that the patient population had a mean age of 65 years, with an elevated body mass index, almost all were hypertensive, almost 30% were diabetic, and 10% had bundle branch block. Echographic parameters indicated that dilated left atrium, and annular and/or valvular calcification were present in half the number of patients. Only 3 of the 146 males had a left ventricular mass $<120\,g/m^2$ and only 1 of the 110 females had $<100\,g/m^2$. The ejection fraction was, nevertheless, >45% in 240 of the 256 patients (93.7%). Given that the majority of these factors have been shown in the general population to be associated with AF,[4,12–15] this high prevalence can be attributable to a confluence of factors and, as such, complicates the evaluation of the influence of renal insufficiency *per se* on the presence of AF.

The patients who presented with AF at the start of dialysis were older and more obese. They had higher pulse pressure, greater left ventricular hypertrophy, greater dimensions of left atrium, and more calcification. All these factors had been associated with AF.[4,7,12–18] Although the association between calcifications and chronic renal disease is well documented,[19,20] as is the relationship between calcifications and disorders of conduction,[21,22,23] there has been only one previous study that has described an association between calcifications and AF.[7] The relationship between female gender and AF that we had observed is not concordant with the findings in previous studies conducted in our own institution; we had either not observed significant differences between the genders or, indeed, had observed a preponderance of males with AF.[8,10]

The incidence of new cases of AF is not only higher than that observed in the general population,[12] but also higher than that described for the population on dialysis. Although there have not been any studies such as ours evaluating the incidence of arrhythmia in patients commencing dialysis, we can make comparisons between our study and those studies that had evaluated the incidence of AF in patients already included in dialysis programs. Our previous study showed an annual incidence of 3.1% in a patient population with a mean time on dialysis of 43 months.[10] The study by Genovesi *et al.*,[11] with a median time on dialysis of 45.2 months, showed an annual incidence of 4.1%. This was 1% in the study by Ansari *et al.*[24] These differences can be attributed to several reasons. First, we need to highlight that in our study, the patients had been followed-up prospectively, with a strict follow-up that would detect any episode of AF that may have occurred. Another important aspect is the age of the population. In our previous study, the mean age of the patients in sinus rhythm was 57 years of age but which, in this study, was 65 years.

Some aspects need to be highlighted in relation to the differences in the clinical profile of the patients who developed arrhythmia in the course of the dialysis compared with those who remained in sinus rhythm. AF has been associated with a greater left atrial size, including in patients on dialysis,[9] but there has always been doubt as to whether this dilation is the cause or the consequence of the AF.[25] There are studies in the general population that have reported atrial dilation as predisposing to the development of arrhythmia,[26] but our study is novel in that it describes this relationship in patients on dialysis.

That ischemic stroke or TIA is present before commencing dialysis and can be a predictive factor in the development of AF is, in our opinion, of considerable clinical interest. It is evident that the AF can only be diagnosed when it is documented, but this does not exclude the possibility that other non-documented episodes may have occurred and which could result in the cerebral ischemia. Our finding can suggest that the patients who had suffered an ischemic stroke or TIA already had the arrhythmia, but that it had not been detected. This implies that the patients who began dialysis with a previous stroke should be followed-up carefully so that those episodes of AF that are brief and self-limiting, but nonetheless thrombogenic, do not pass unnoticed. New equipment of continuous electrographic monitoring[27] can have an important role as a diagnostic tool in this group of patients.

Valvular calcifications constitute a factor that is independently associated with clinical evolution of AF. The most notable aspect in our analysis, nevertheless, was that the most important independent predictive factor in the development of arrhythmia that we had observed was the presence of bundle branch block at the commencement of dialysis. In a recent study carried out in our center, we noted that branch block is a very prevalent finding in the population on dialysis.[23] Nevertheless, there are no studies, in patient population on dialysis, which relate disturbances in intraventricular conduction with the presence of AF. In this study, its presence at the start of dialysis increases the probability of developing the arrhythmia over the clinical course of the dialysis by sixfold.

The presence of AF has had an evident influence on survival in our patients. In two studies previously conducted in our own institution, AF represented a 2.1-fold increase in mortality risk[28] and, in the other study, the mortality rates in the first and second year of follow-up were 38 and 53%, respectively, in the AF group and 14 and 31%, respectively, in the sinus rhythm group.[10] In the Genovesi *et al.* study[11] the incremental all-mortality risk that implied the presence of AF was quantified as being 1.65-fold and, from cardiovascular cause, it was 2.15-fold. The influence of AF on the patients who commenced dialysis is not very different from that pertaining to the general population,[29–31] although there is an increase in the mortality risk that is already very elevated.

Atrial fibrillation has a clear importance in the clinical evolution of ischemic cerebrovascular accident. In our study, the presence of AF increased the probability of developing an ischemic stroke by 9.8-fold. The Framingham study places this at fivefold in the general population.[32] The results of this study are not in agreement with the scarce information available in the literature.[11,33] The recent study by Genovesi *et al.*[11] did not observe an increased risk associated with the presence of AF. We believe that one of the reasons could be the different methodologies employed. For example, Genovesi *et al.* considered presenting with a stroke as that occurring within the overall time period of the 3 years of their study. However, many patients had died during this period. If we take into account that the patients with AF had a mortality rate significantly higher than the patients in sinus rhythm, and that the mortality in the first years in patients with AF was 31%,[9] then the time over which the patients with AF had been exposed to the risk of stroke was lower. All of our published studies had analyzed the risk of presenting with an ischemic stroke only during the period in which the patients were followed-up and, in all of them, the AF increased the risk of the event. The increase in risk in this study (9.8-fold) is higher than that encountered in our other studies in which the patients with AF were observed to have a 4.6-fold[31] or 5.2-fold[10] increase in the probability of suffering a thromboembolic event. Our opinion, supported by the results of this and other previous studies,[8,10,31] is that AF constitutes an important thromboembolic risk factor not only in the general population, but in patients with end-stage renal disease as well. This implies that antithrombotic therapy needs to be implemented if the risk of these complications is to be reduced. The question that remains to be answered is whether the patients with AF on dialysis need to be treated with oral anticoagulants. The studies that had evaluated the benefit of anticoagulant therapy for patients with AF had excluded patients with end-stage renal disease and, as such, the risk–benefit relationship of the therapy in this population has not been evaluated. Classically, chronic renal insufficiency with anticoagulant therapy has been associated with a high risk of bleeding. However, this risk has not been established within the context of current conditions of efficacy and quality of dialysis. In a retrospective study conducted in our center,[34] the use of anticoagulant treatment resulted in a 2.3-fold increase in the risk of bleeding. However, this increase was not related to fatal intracranial hemorrhage or associated sequelae. The only recent study that analyzed the repercussion of anticoagulation on the clinical evolution of the patients on dialysis was carried out by Abbot *et al.*,[35] and their results indicated a clear benefit. Alternative therapeutic options can be the use of antiplatelet agents, but these are not exempt from hemorrhagic risk either.[36] Opinions vary, and there are some who consider that the current recommendations for the general population are not applicable to patients on dialysis, that is, that the patients with AF on dialysis are not to be treated with anticoagulants.[37,38] Our opinion is that, in patients with chronic renal insufficiency being treated with dialysis, the increase in the risk of bleeding does not

constitute an *a priori* contraindication to oral anticoagulant treatment. However, earlier evaluation of the embolic and hemorrhagic risk is necessary in each patient. This recommendation is consistent with the data from two recent analyses[6,39] which indicated that treatment with warfarin should be considered in the prevention of thromboembolism in patients with AF undergoing dialysis.

In addition to the inherent limitations of a single-center study, we cannot discard the possibility of brief and self-limited asymptomatic episodes passing unnoticed and, as such, the frequency of AF would be higher. On the other hand, in the group of patients starting dialysis with non-permanent AF, the different clinical patterns of presentation had not been analyzed as it had not been possible to determine the number of episodes in all the cases and whether sinus rhythm had spontaneously recovered. Hence, in the echocardiographic assessments, we did not take into account the time of the measurements in relation to the dialysis sessions and, as such, the assessments were not carried out in all the patients under similar loading conditions.

PATIENTS AND METHODS

All procedures were conducted within the guidelines of Good Clinical Practice, and all patients provided informed consent to participate in the study.

The design of the study was prospective and observational. To establish the prevalence of AF in the patients who commence dialysis, we evaluated all those who began dialysis (hemodialysis or peritoneal dialysis) between 1 November 2003 and 15 September 2007 in our hospital and its satellite health-care centers.

Excluded from the study were those who had commenced treatment in centers not associated with our institution, had previously received a kidney transplant, those who had recovered renal sufficiency and did not need dialysis, and those who, within the first few sessions of dialysis, had died or changed residence to outside our clinical catchment area.

Atrial fibrillation was considered when the arrhythmia was permanent or had been documented in any of our electrocardiographic databases. Follow-up of the patients continued up to 30 May 2008 or until death, renal transplant, or change of residence beyond our remit of dialysis provision had taken place. The patients were treated according to the attending physician with no specific recommendation with respect to the treatment of the arrhythmia or antithrombotic medications.

An electrocardiogram was scheduled to be carried out annually and, as well, at any time that the patient had any symptoms that suggested the presence of arrhythmia, or if alterations in the rhythm were detected in the course of the dialysis session. The incidence of AF was established in those patients who, at the time of inclusion into the study, were in sinus rhythm and in whom the presence of arrhythmia had not been noted. Arrhythmia was considered when documented, irrespective of the number of episodes or of the clinical pattern of presentation.

All the patients had an evaluation within the first month of placement on dialysis. This included cardiological clinical history, electrocardiogram, the measurement of hematological and biochemical parameters, and a color Doppler echocardiogram. The factors associated with, or predisposing to, AF were measured and so was the influence of the arrhythmia on ischemic stroke and mortality. The variables measured included age, gender, smoking habit, body mass index, pulse pressure, diabetes, arterial hypertension, bundle branch block, presence of previously documented coronary disease (myocardial infarction or coronary lesions $>70\%$ in the coronary angiography), presence of ischemic stroke, TIA, or previous peripheral embolism. Hematological parameters measured included hemoglobin, hematocrit, and platelets. Biochemical parameters measured included urea, creatinine, albumin, cholesterol, triglycerides, CRP, intact parathormone, calcium, phosphorus, ferritin, transferrin, glycosylated hemoglobin, and homocysteine. Color Doppler echocardiography was used to measure the following parameters: left atrial size, left ventricular dimensions, left ventricular mass, left ventricular ejection fraction, ascending aorta dimension, presence of annular and/or valvular calcifications, and E/A ratio in mitral filling flow. The presence of AF in the course of dialysis was noted in relation to whether the patients were on hemodialysis or peritoneal dialysis. Patients were recorded as having hypertension or diabetes if, at the time of inclusion into the study, they were receiving treatment for the control of these diseases.

Statistical analyses

The Student's *t*-test or the non-parametric Mann–Whitney test was used in the descriptive analysis of the data. Comparison of qualitative variables was carried out with Pearson's χ^2 test. Univariate and multivariate analyses were carried out on all measured variables. The objective prognostic variable of this study was the occurrence of the event or diagnosis of AF in the follow-up. The study was based on an analysis of the predictors at the start of treatment using Cox's regression of proportional risk. The variables included were those that, in the overall patient group, were statistically significant in univariate analysis, as well as those that were not statistically significant, but were of clinical relevance. The same assessment was applied with respect to death or presence of ischemic stroke in the course of dialysis. The best predictive model was obtained using the procedure of progressive conditional incorporation. The odds ratio and the 95% confidence interval were calculated. Survival analysis was carried out comparing Kaplan–Meier curves using the log-rank test. In all tests, a probability of $P<0.05$ was considered as statistically significant.

DISCLOSURE

All the authors declared no competing interests.

REFERENCES

1. Zoccali C, Mallamaci F, Tripepi G. Traditional and emerging cardiovascular risk factors in end-stage renal disease. *Kidney Int* 2003; **63**: S105–S110.

2. Dikow R, Adamczak M, Henriquez DE *et al.* Strategies to decrease cardiovascular mortality in patients with end-stage renal disease. *Kidney Int* 2002; **61**: S5–S10.
3. Ezekowitz MD. Atrial fibrillation: the epidemic of the new millennium. *Ann Intern Med* 1999; **131**: 537–538.
4. Go AS, Hylek EM, Phillips KA *et al.* Prevalence of diagnosed atrial fibrillation in adults. National implications for rhythm management and stroke prevention. The anticoagulation and risk factors in atrial fibrillation (ATRIA) study. *JAMA* 2001; **285**: 2370–2375.
5. Korantzopoulos P, Kokkoris S, Liu T *et al.* Atrial fibrillation in end-stage renal disease. *Pacing Clin Electrophysiol* 2007; **30**: 1391–1397.
6. Reinecke H, Brand E, Mesters R *et al.* Dilemmas in the Management of Atrial Fibrillation in Chronic Kidney Disease. *J Am Soc Nephrol* 2009; **20**: 705–11.
7. Atar I, Konas D, Acikel S *et al.* Frequency of atrial fibrillation and factors related to its development in dialysis patients. *Int J Cardiol* 2006; **106**: 47–51.
8. Vazquez E, Sanchez-Perales C, Borrego F *et al.* Influence of atrial fibrillation on the morbido-mortality of patients on hemodialysis. *Am Heart J* 2000; **140**: 886–890.
9. Genovesi S, Pogliani D, Faini A *et al.* Prevalence of atrial fibrillation and associated factors in a population of long-term hemodialysis patients. *Am J Kidney Dis* 2005; **46**: 897–902.
10. Vázquez-Ruiz de Castroviejo E, Sánchez-Perales C, Lozano-Cabezas C *et al.* Incidence of atrial fibrillation in hemodialysis patients. A prospective long-term follow-up study. *Rev Esp Cardiol* 2006; **59**: 779–784.
11. Genovesi S, Vincenti A, Rossi E *et al.* Atrial fibrillation and morbidity and mortality in a cohort of long-term hemodialysis patients. *Am J Kidney Dis* 2008; **51**: 255–262.
12. Heeringa J, van der Kuip DA, Hofman A *et al.* Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. *Eur Heart J* 2006; **27**: 949–953.
13. Kannel WB, Wolf PA, Benjamin EJ *et al.* Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. *Am J Cardiol* 1998; **82**: 2N–9N.
14. Okin PM, Wachtell K, Devereux RB *et al.* Regression of electrocardiographic left ventricular hypertrophy and decreased incidence of new-onset atrial fibrillation in patients with hypertension. *JAMA* 2006; **296**: 1242–1248.
15. Psaty BM, Manolio TA, Kuller LH *et al.* Incidence of and risk factors for atrial fibrillation in older adults. *Circulation* 1997; **96**: 2455–2461.
16. Mitchell GF, Vasan RS, Keyes MJ *et al.* Pulse pressure and risk of new-onset atrial fibrillation. *JAMA* 2007; **297**: 709–715.
17. Lentine KL, Rocca-Rey LA, Bacchi G *et al.* Obesity and cardiac risk after kidney transplantation: experience at one center and comprehensive literature review. *Transplantation* 2008; **86**: 303–312.
18. Tsang TS, Barnes ME, Miyasaka Y *et al.* Obesity as a risk factor for the progression of paroxysmal to permanent atrial fibrillation: a longitudinal cohort study of 21 years. *Eur Heart J* 2008; **29**: 2227–2233.
19. Maher ER, Pazianas M, Curtis JR. Calcific aortic stenosis: a complication of chronic uraemia. *Nephron* 1987; **47**: 119–122.
20. Mazzaferro S, Coen S, Bandini I *et al.* Role of ageing, chronic renal failure and dialysis in the calcification of mitral annulus. *Nephrol Dial Transplant* 1993; **8**: 335–340.
21. Mellino M, Salcedo EE, Lever HM *et al.* Echographic-quantified severity of mitral annulus calcification: prognostic correlation to related hemodynamic, valvular, rhythm, and conduction abnormalities. *Am Heart J* 1982; **103**: 222–225.
22. Nair CK, Runco V, Everson GT *et al.* Conduction defects and mitral annulus calcification. *Br Heart J* 1980; **44**: 162–167.
23. Vázquez Ruiz de Castroviejo E, Sánchez Perales C, López López J *et al.* Prevalence of and predisposing factors for bundle branch block in patients starting dialysis. *Rev Esp Cardiol* 2008; **61**: 719–725.
24. Ansari N, Manis T, Feinfeld DA. Symptomatic atrial arrhythmias in hemodialysis patients. *Ren Fail* 2001; **23**: 71–76.
25. Dittrich HC, Pearce LA, Asinger RW. Stroke prevention in atrial fibrillation investigators left atrial diameter in non-valvular atrial fibrillation: an echocardiographic study. *Am Heart J* 1999; **137**: 494–499.
26. Tsang TS, Barnes ME, Bailey KR *et al.* Left atrial volume: important risk marker of incident atrial fibrillation in 1655 older men and women. *Mayo Clin Proc* 2001; **76**: 467–475.
27. Sarkar S, Ritscher D, Mehra R. A detector for a chronic implantable atrial tachyarrhythmia monitor. *IEEE Trans Biomed Eng* 2008; **55**: 1219–1224.
28. Vázquez E, Sánchez-Perales C, Lozano C *et al.* Comparison of prognostic value of atrial fibrillation *versus* sinus rhythm in patients on long-term hemodialysis. *Am J Cardiol* 2003; **92**: 868–871.
29. Benjamin EJ, Wolf PA, D'Agostino RB *et al.* Impact of atrial fibrillation on the risk of death. The Framingham heart study. *Circulation* 1998; **98**: 946–952.
30. Stewart S, Carole LH, Hole DJ *et al.* A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Oausket study. *Am J Med* 2002; **113**: 359–364.
31. Vidalillet H, Granada JF, Chyou PH *et al.* A population-based study of mortality among patients with atrial fibrillation or flutter. *Am J Med* 2002; **113**: 365–370.
32. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991; **22**: 983–988.
33. Wiesholzer M, Harm F, Tomasec G *et al.* Incidence of stroke among chronic hemodialysis patients with non-rheumatic atrial fibrillation. *Am J Nephrol* 2001; **21**: 35–39.
34. Vazquez E, Sanchez-Perales C, Garcia-Cortes MJ *et al.* Ought dialysis patients with atrial fibrillation be treated with oral anticoagulants? *Intern J Cardiol* 2003; **87**: 135–139.
35. Abbott KC, Trespalacios FC, Taylor AJ *et al.* Atrial fibrillation in chronic dialysis patients in the United States: risk factors for hospitalization and mortality. *BMC Nephrol* 2003; **4**: 1.
36. Sanchez-Perales C, Vazquez E, Garcia-Cortes MJ *et al.* Antiplatelet therapy and risk of bleeding in hemodialysis patients. *Nefrología* 2002; **5**: 456–462.
37. To AC, Yehia M, Collins JF. Atrial fibrillation in haemodialysis patients: do the guidelines for anticoagulation apply? *Nephrology (Carlton)* 2007; **12**: 441–447.
38. Bennet WM. Should dialysis patients ever receive warfarin and for what reasons? *Clin J Am Soc Nephrol* 2006; **1**: 1357–1359.
39. Quinn RR, Naimark DM, Oliver MJ *et al.* Should hemodialysis patients with atrial fibrillation undergo systemic anticoagulation? A cost-utility analysis. *Am J Kidney Dis* 2007; **50**: 421–432.